

Applicants: Jonathan A. Bard, et al.
U.S. Serial No. 09/430,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS
Sheet 1 of 19

*1/19* .

	FIGURE 1A			
	-80	09-	-40	
-28	AGTATTGTTTGTCTGTTGGGGCGTCATCCCTCAAGTGTATCACTTAGTTCAA	GTAGGGCGTCATCCCTCAAGT	GTATCACTTAGTTCAA	31
	-20	-1	20	
32	GAGTCCTGGAATCTTTCACATCCACTATGAACACCTCTCACCTCCTGGCCTTGCTGCTC  M N T S H L L A L L L	CACTATGAACACCTCTCACCT M N T S H L	CTCTCACCTCCTGGCCTTGCTGCTC S H L L A L L L	91
	40	09	80	
92	CCAAAATCTCCACAAGGTGAAAACAGCAAACCCCTGGGCACCCCATACAACTTCTCT P K S P Q G E N R S K P L G T P Y N F S	GAAAACGAAACCCCTGGGCACCCCATACAA	CCCATACAACTTCTCT P Y N F S	151 31
	100	120	140	
152 32	GAACATTGCCAGGATTCCGTGGA	TTCCGTGGACGTGTCTTCATCGTCACTTCCTACAGCATTGAGS V D V M V F I V T S Y S I E	TTCCTACAGCATTGAG S Y S I E	211 51
	160	180	200	
212 52	ACTGTGGGGGGTCCTGGGTAA	CCTGGGTAACCTCTGCTGATGTGTGTGACTGTGAGGAGGAG	TGTGAGGCAGAAGGAG V R Q K E	271



Applicants: Jonathan A. Bard, et al.
U.S. Serial No. 09/430,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS
Sheet 2 of 19

## 2/19

		rgrgc 331 C 91		GAGAG 391 E 111		rcrcg 451 S 131		AGCCC 511 P 151		rcrcc 571 s 171
	260	CTGCTTATCGCCAACCTGGCCTTCTCTGACTTCCTCAI	320	GCCGTCTACACCATCATGGACTACTGGATCTTTGG A V Y T I M D Y W I F G	380	CATCCAGTGCATGTCGGTCTCCATCCT	440	CAGCTCATCAACCCAACAGGCTGGAA	200	TGTGCTCATCTGGGTCATTGCCTGTGTCCTCT
	240	AAAGCCAACGTGACCTGCTTATCGCCAACCTGGCCTTCTCTGACTTCCTCATGTGC K A N V T N L L I A N L A F S D F L M C	300	CTCCTCTGCCAGCCGCTGACCGCCGTCTACCATGGACTACTGGATCTTTGGAGAGAGA	360	ACCCTCTGCAAGATGTCGGCCTTCATCCAGGTCGTCGTCGTCGTCCTCTCGTCTCTTCGTTCCTCTCTCTTCGTTGCCAAGATGTCGGTCAAGATGTCGGTGAAGGTTCTCCATCCTCTCTCT	420	ggagaggcat E R H	480	AGCATCTCACAGGCCTACCTGGGATTGTGCTCATCTGGGTCATTGCCTGTGTCTCTCC S I S Q A Y L G I V L I W V I A C V L S
FIGURE 1B	220	AAAGCCAACGTGACCAA K A N V T N	280	CTCCTCTGCCAGCCGCT L L C Q P L	340	ACCCTCTGCAAGATGTC T L C K M S	400	CTCGTCCTCGTGGCCCT	460	AGCATCTCACAGGCCTA S I S Q A Y
		272		332 92		392 112		452 132		512 152

FIGURE 1C

Applicants: Jonathan A. Bard, et al.
U.S. Serial No. 09/430,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS
Sheet 3 of 19

3/19

	631 191		691		751 231		811 251		871 271
260	CTGCCCTTCCTGGCATCTTCTTCCACAGAACCACTCCAAGGCT L P F L A N S I L E N V F H K N H S K A	620	CTGGAGTTCCTGGCAGATAAGGTGGTCTGTACCGAGTCCTGGCCACTGGCTCACCACCGC	089	ACCATCTACACCATCTTCCAGTACTGCCTCCCACTGGGCTTCATCCTG	740	GTCTGTTATGCACGCATCTACCGGCGCCCTGCAGGGCAGGGCGCGCGTGTTTCACAAGGGC V C Y A R I Y R R L Q R Q G R V F H K G	800	ACCTACAGCTTGCGACATGAAGCAGGTCAATGTGGTGCTGGTGGTGATGGTGTTGTTGTTGTTGTTGTTGTTGTTGTT
540	CCAACAGCATCCTGGAG	009	SCAGATAAGGTGGTCTGT	099	ACCTTCCTGCTCTTC	720	CGCATCTACCGGCGCCTG R I Y R R L	780	CGAGCTGGGCACATGAAG R A G H M K
520	CTGCCCTTCCTGG	580	CTGGAGTTCCTGG	640	ACCATCTACACCA T I Y T T	700	GTCTGTTATGCAC V C Y A F	760	
	572 172		632 192		692 212		752 232		812 252



860

FIGURE 1D

Applicants: Jonathan A. Bard, et al.
U.S. Serial No. 09/430,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS
Sheet 4 of 19

# 4/19

GTGGCCTT	GTGGCCTTTGCCGTGCTGCTCTGCATGTTCAACAGGCCTGGAAGACTGGCAC V A F A V L W L P L H V F N S L E D W H	CCTGGAAGACTGGCAC L E D W H	931 . 291
088	006	920	
CATGAGGCCATCCCCATCTGCCACGGGAACCTCATTTTTTAGTGTGCCACTTGCTTG	GGGAACCTCATCTTAGTCG N L I F L V	STGCCACTTGCTTGCC C H L L A	991 .
940	096	086	
ATGGCCTCCACCTGCGTCAACCCATTCATCTATGGCTTTCTCAACACCAACTTCAAGAAG M A S T C V N P F I Y G F L N T N F K K	rtcatctatgctttctcaag	SACCAACTTCAAGAAG T N F K K	1051 331
1000	1020	1040	
GAGATCAAGGCCCTGGTGCTGACTTGCCAGCAGAGCGCCCCCCTGGAGGAGTCGGAGCAT E I K A L V L T C Q Q S A P L E E S E H	GCTGACTTGCCAGCAGAGCGCCCCCCTGGAGGAGTCGGAGC	GAGGAGTCGGAGCAT E E S E H	1111 351
1060	1080	1100	
CTGCCCCTGTCCACAGACTACGGAAGTCTCCAAAGGGTCCCTGAGGCTAAGTGGCAGG	SAAGTCTCCAAAGGGTCCCTC  V S K G S L	; AGGCTAAGTGGCAGG R I, S G R	1171



Applicants: Jonsthan A. Bard, et al.
U.S. Serial No. 09/430,775
Füing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS

Sheet 5 of 19

	1231 375		1291
	GGCTCTTC		GCTTTCTG
1160	Atgrecttgeea	1220	CCCAGCATTCCTG
1140	ccaggtctaggtctrcccrgccatgtcccrtgccaggcrctrc	1200	GCACACTGCAAGCTGGGTGGCACCCCAGCATTCCTGGCTTTCTG
1120	TCCAATCCCATTTAA(S N P I *	1180	CACTTAGCTAAGTGG
	172 372		232

FIGURE 1E

Sheet 6 of 19

6/19

FIGURE 2A

150 200 100 QLIINPRGWR QLIINPRGWR IFTLALAYGA IFTLALAYGA IFTLALAYGA QLIINPRGWR LAAFKDKYV LAAFKDKYV **OLIINPTGWK** MVFIVTSYSI CLLCOPLTAV ALEFLADKVV AVMCLPFTFV LDAYKDKY AIMCLPFTF AVMCLPFTF II SEHCODSVDV NESFSDLLV ENVFHKNHSK NDDCHLPLAU VNLSFSDLLV NDDCHLPLAV MISFSDLLV TDEPFONT. NDDCHLPLAM ANLAFSDFLM SLVLVALERH SLVLIAVERH SLVLIAVERH SLVLIAVERH TDEPFONVS. TDEPFONVS. **QCVSITVSIF** SKPLGTPYNF EKNAQLLAFE QCVSITVSIF SLPFVIYQIL E. NSPFLAFE E. NSPLLAFE QCMSVTVSIL QCVSITVSIF STAPELANSIL SLPFLIYOVM SLPFVIYOIL EMRNVTNILL EKANVTNLLL EMRNVTNILI EMRNVINILI III TVIWVLAVAS TVIWVLAVAS LPKSPQGENR AVIWVLAVAS ENHSVHSNFS ETMCKLNPFV VLIWVIACVL ENYSVHYNVS ENHSIHYNAS CIMCUTUROR LIIIILKOK EAMCKLNPFV ETMCKLNPFV ALIIIIKOK ALIIIILKOK ETLCKMSAFI MNTSHLLALL STLFSOV STLFSRV VIILGVSGNL VIILGVSGNL YTIMDYWIFG **YTLMDHWVFG** TIMDHWVFG YTLMDHWVFG PNNRHAYVGI PNNRHAYICI PNNRHAYIGI VIILGUSGNL PSISOAYLGI STLFSKV ETVVGVLGNL 101 151 51 mouse Y1 mouse Y1 human Y1 mouse Y1 human Y1 mouse Y1 human Y1 human Y1 rat Y1 rat Y1 rat Y1 rat Y1 hp25a hp25a hp25a hp25a

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U.S. Serial No. 09/430,775
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Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS

7/19

350 300 250 COCSAPLEES WNHOITATCN WNHOITATON CDFRSRDDDY CDFRSRDDDY CDFRSRDDDY CKRRNNMMDK WNHOITATON QROGRVFHR LKRRNNMMDK WHEALPICH KRRNNMMDK QRDLQFFFNF QRDLQFFFNF QRDLQFFFNF PLTIFNTVFD KKEIKALVLT FICYFKIYIR PLTIFNTVFD PLTIFNTVFD LVCYARIYRR PLHVFNSLED FICYFKIYI FICYFKIYI FIYGFLNTNF MVVAFAVLWL I FYGFLNKNF IFYGFLNKNF I FYGFLNKNF OYFGPLCFI LOYFGPLCFI QYFGPLCFI IVVAFAVCWL IVVAFAVCWL IVVAFAVCWL TKRINVMLLS TAMISTCVNP TAMISTCVNP TAMISTOWN TKRINIMLLS TKRINIMLLS LAMASTCVNP RLSYTTLLEV RLSYTTLLLV RLSYTTLLEV MKQVNVVLVV VII GTYS. LRAGH MRDNKYRSSE IRDSKYRSSE IRDSKYRSSE CTESWPLAHH CFDKFPSDSH GNIIFIVCHE HNLLFLLCHL HNLLFLCHL CFDKFPSDSH CFDQFPSDSH HNLLFLLCH 251 301 201 Y1 Y1 Y1 Y1 X human Y1 rat Y1 rat Y1 rat Y1 mouse human mouse human mouse hp25a hp25a hp25a

FIGURE 2B

Applicants: Jonathan A. Bard, et al.
U.S. Sertal No. 09/436,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS

8/19

388

N. DNEKV\* NDDNEKI \* N. DNEKI\* SPVAFKKINN SPVAFKKISM SPVAFKKISM GRSNPI\*.. DVSKTSLKQA DVSKTSLKQA DVSKTSLKQA TVSKGSLRLS ETIAMSTMHI ETIAMSTMHT EHLPLSTVH

351

human Y1

hp25a

mouse Y1 rat Y1

FIGURE 2C



Applicants: Jonathan A. Bard, et al.
U.S. Serial No. 09/430,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS
Sheet 9 of 19

9/19

## FIGURE 3A

	-:	170						-15	50					•	-130	)				
ΑT	rag(	CTCI	· rcai	AGC	CAT	AAG2	ATA	raa:	GTA	· GCTZ	AAG	AAT:	rgt(	CTC	CCT	CTCC	CCTO	STC	CCTT	'G
	- 1	110						- 9	90						-70	)				
TI	CTI	raco	· CTG(	GTT(	CCA.	rtt:	FAC	ATG(	CCTO	: GGA(	CCT	rtg <i>i</i>	AGTI	rccz	\TTT	GTI	rtgi	TTT	rgca	'G
	#	-50	)	•				•	-30						-1	ĽO				
GC	TAC	CACI	CAC	SAAC	GTG	GCC	CCTI	OAT?	GTC1	· rtg/	AAG:	rtco	CTGC	TCI	TCI	CAC	ACC	CAC	CAT	Ġ
																			M	
		10	)						30			•			5	0				
AA	TAC	CTC	· TCA	TC	rcai	GGC	CCTC	CCI	TTTC	· CTCC	CGGC	CATI	CCI	'ACA	AGG	TAA	G <b>A</b> A	TGG	GAC	c
N	T	s	Н	L	M	A	s	L	S	P	A	F	L	Q	G	K	N	G	T	
		70						,	90						11	0				٠.
AA	CCC	ACT	· GGA	TTC	CCI	· CTA	TAA	TCI	CTC	· :TGA	\CG0	CTG	CCA	.GGA	TTC	GGC	AGA	TCT	GTT	G
N	P	L	D	S	L	Y	N	L	s	D	G	C	Q	D	s	A	D	L	L	•
	1	30	:		÷			15	0					~	170					
GC	CTT	CAT	CAT	CAC	CAC	CTA	.CAG	CGT	TGA	GAC	CGT	'CTT	GGG	GGT	CCT	AGG	AAA	CCT	CTG	C
A	F	I	I	Т	T	Y	s	V	E	Т	V	L	G	V	L	G	N	L	С	
		190	•			•		2	10				•		23	0 .			,	•
TT(	GAT	ATT	TGT	GAC	CAC	AAG	GCA	AAA	GGA	AAA	GTC	CAA	TGT	GAC	CAA	CCT	ACT	CAT	TGC	3
•	т	172	37	т.	•	D	$\sim$	T.F	13	7.7	C	NT	37	T.	<b>N</b> T	т	т .	_	7	

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U.S. Serial No. 09/430,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS

Sheet 10 of 19

### 10/19

#### FIGURE 3B

290 250 270 AACCTGGCCTTCTCTGACTTCCTCATGTGTCTCATCTGCCAGCCGCTCACGGTCACCTAC L I C 0 P Т V F L M C F S D N 350 330 310 ACCATCATGGACTACTGGATCTTCGGCGAAGTCCTTTGCAAGATGTTAACGTTCATCCAG C K М L T F F G E V L Y W I M D410 390 370 TGTATGTCGGTGACAGTCTCCATCCTCACTGGTCCTTGTGGCCCTGGAGAGGCACCAG V L Ε R S. L V L Α I L Т V S C S V 470 450 430 CTCATTATCAACCCGACTGGCTGGAAACCCAGCATTTCCCAGGCCTACCTGGGGATTGTG Q Y L G I Ι P Т G W K P S Ι S Α N 510 530 490 GTCATCTGGTTCATTTCTTGTTTCCTCTCCTTGCCCTTCCTGGCCAATAGCATCCTGAAC N S Ι F s L P F L Α S C L Ι W F Ι 590 570 550 GACCTCTTCCACTACAACCACTCTAAGGTTGTGGAGTTTCTGGAAGACAAGGTTGTCTGC F L E D K V ·C S K V V E D L F Н Y N Η 650 630 610 TTTGTGTCCTGGTCCTCGGATCACCACCGCCTCATCTACACCACCTTTCTGCTGCTCTTC F F L L S S D Н Η R L Ι Y T F V S



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U.S. Serial No. 09/430,775
Filing Date: October 29, 199
Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS

Sheet 11 of 19

### 11/19

### FIGURE 3C

710 690 670 М R Ι Y R L V C Y P  $\mathbf{L}$ Α F Ι C V 770 750 730 CAGAGGCAGAGGCGTGCGTTCCACACGCACACTTGCAGCTCACGAGTGGGGCAGATGAAG K T C S S R V G F Η Т Η R A R 0 R 830 810 790 CGGATCAATGGCATGCTCATGGCAATGGTGACTGCCTTTGCAGTTCTCTGGCTGCCCCTG L F T Α A M V R Ι N G L M A 890 870 850 CATGTGTTCAACACTCTGGAGGACTGGTACCAGGAAGCCATCCCTGCTTGCCATGGCAAC N E D W Y Q Ε A Ι P C Т F L 950 930 910 CTCATCTTCTTGATGTGCCACCTGTTTTGCCATGGCTTCCACCTGTGTCAACCCTTTCATC Ι S Т C L F A. M Α C Η L M 990 1010 970 TATGGCTTTCTCAACATCAACTTCAAGAAGGACATCAAGGCTCTGGTTCTGACCTGCCGT V C R K Α L L N I N K K D Ι Ġ F L 1070 1050 1030 TGCAGGCCACCTCAAGGGGAGCCTGAGCCTCTGCCCCTGTCCACTGTGCACACGGACCTC L T D Ε P L P L S Т V Η G E P P R P



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Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS

12/19

TCCAAGGGATCTATGAGGATGGGTAGCAAGTCTAACGTCATGTAGTCATGTCTAGGCTCT 1190 Σ Z വ 1170 × വ Ö Σ 召 Σ ഗ 1150 Ö × ß

1110

1090

FIGURE 3D

GTATCATCCTGCCATTTCTGGTCTTTGGGGCCCAGACGGCGGCAAGAGACTTGAAGCTT

1250

TCCGCCATTTTCTTTCGACACACCCTTTCACTGAGCTAAGTAGACACAATGCAAGCTGTG

1210

1230



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Title of the Invention: METHOD OF OBTAINING
COMPOSITIONS AND COMPRISING Y4 SPECIFIC
COMPOUNDS

Sheet 13 of 19

Sheet 13 of 19

## 13/19

### FIGURE 4

	1				50
Y4rat	MNTSHLMASL	SPAFLQGKNG	TNPLDSLYNL	SDGCQDSADL	LAFIITTYSV
Y4hum	MNTSHLLALL	LPKSPQGENR	SKPLGTPYNF	SEHCODSVDV	MVFIVTSYSI
	51	•	·		100
-	<u> </u>		<del></del>		- II
Y4rat	BTVLGVLGNL	CLIFVTTRQK	BKSNVTNLLI	ANLAFSDFLM	CLICQPLTVT
					CLLCQPLTAV
	101				150
			III _		
Y4rat	YTIMDYWIFG	EVLCKMLTFI			QLIINPTGWK
		ETLCKMSAFI			
	151				200
		ıv			
Y4rat	·-	VVIWFISCFL	=	NDLFHYNHSK	VVEFLEDKVV
	_	VLIWVIACVL			
	201				250
			v	<del></del>	
Y4rat	CFVSWSSDHH	RLIYTTFLLL	FQYCVPLAFI	LVCYMRIYOR	LORORRAFHT
Y4hum	CTESWPLAHH	RTIYTTFLLL	FOYCLPLGFI	LVCYARIYRR	LQRQGRVFHK
	251				300
			vi		
Y4rat	HTCSSRVGQM	KRINGMLMAM	VTAPAVLWLP	LHVFNTLEDW	YQEAIPACHG
					HHEAIPICHG
	301				350
		- vii			
Y4rat		AMASTCVNPF	•	KDIKALVLTC	RCRPPOGEPE
		AMASTCVNPF			<del></del>